Benefit-Risk Of arterial THrombotic prEvention with Rivaroxaban for atrial fibrillation in daily clinical practice. A French cohort within the nationwide claims and hospital database (BROTHER).

First published: 02/08/2016

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS14567

Study ID

49822

DARWIN EU® study

No

Study countries

☐ France

Study description

The research question is to assess the one-year and two-year benefit-risk of rivaroxaban for stroke prevention in atrial fibrillation (SPAF) compared to vitamin K antagonists (VKA) and dabigatran among new anticoagulant users. The main objective is to compare the one-year and two-year risk of the following individual outcomes: stroke and systemic embolism (SSE), major bleeding and death, between new users of anticoagulant for SPAF during drug exposure: rivaroxaban versus VKA, and rivaroxaban versus dabigatran (standard and reduced doses). Secondary outcomes were clinically relevant bleeding (CRB), acute coronary syndrome (ACS) and a composite criterion of SSE, major bleeding or death. This is a cohort study in the French national healthcare claims and hospitalisation database (SNDS, Système National des Données de Santé) including new users of rivaroxaban, dabigatran, or VKA for SPAF with a follow-up for at least one year and up to two years per subject, and three-year history. The index date will be that of the first dispensation of rivaroxaban, dabigatran, or VKA in 2013 or 2014. Data will be extracted from 2010 to 2015. Outcomes analysis will be performed during drug exposure for matched patients on high-dimensional propensity score (hdPS), and all patients with hdPS adjustment.

Study status

Finalised

Research institutions and networks

Institutions

Bordeaux PharmacoEpi, University of Bordeaux

France

First published: 07/02/2023

Last updated: 08/02/2023

Institution | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Contact details

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Study contact

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Primary lead investigator

Nicholas Moore

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 01/02/2016

Study start date

Actual: 24/08/2016

Data analysis start date

Actual: 16/11/2016

Date of final study report
Actual: 20/11/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Bayer Pharma AG

Study protocol

BROTHER_ENCePP_Protocol_V1.0_20181203.pdf (7.17 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The main objective is to compare the one-year and two-year risk of the following individual outcomes: SSE, major bleeding and death between new users of anticoagulant for SPAF during drug exposure: rivaroxaban versus VKA, and rivaroxaban versus dabigatran (standard and reduced doses).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AA) Vitamin K antagonists

Vitamin K antagonists

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

Medical condition to be studied

Atrial fibrillation

Population studied

Short description of the study population

The study focused on subjects with a specific or sensitive diagnosis of non-valvular Atrial Fibrillation (NVAF) and a first reimbursed dispensation of rivaroxaban, dabigatran, or vitamin K antagonists in 2013 or 2014, and no previous anticoagulant dispensation in the previous three years. Two NVAF cohorts was defined: a specific cohort for main analysis to minimize the risk of false positives, and a sensitive cohort for secondary analysis to minimize the risk of false negatives.

Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

Non valvular atrial fibrillation patients

Estimated number of subjects

150000

Study design details

Outcomes

SSE as a hospitalisation with primary diagnosis of ischemic/undefined stroke, or other systemic arterial embolism or surgical procedure for systemic arterial embolism, Major bleeding as a hospitalisation with primary diagnosis of haemorrhagic stroke or other critical organ or site bleeding, or other bleeding with blood transfusion during hospital stay, or resulting in death, All-cause of death. Composite of SSE, major bleeding and death, CRB as a hospitalisation with primary diagnosis of haemorrhagic stroke (linked or associated diagnosis also included), or other critical organ or site bleeding, or gastro-intestinal or urogenital or other bleeding, ACS as a hospitalisation with main diagnosis of myocardial infarction or unstable angina, drug use, Healthcare resources use and costs.

Data analysis plan

Statistical analysis will be carried out according to a documented and approved Statistical Analysis Plan (SAP). The SAP describes statistical analysis as foreseen at the time of planning study. Statistical analysis will be performed after database lock using SAS® software. Blind double programming will be used for main outcome measures.Primary outcomes will be analysed using survival

methods: Kaplan-Meier estimate or cumulative incidence function estimate for cumulative incidence of clinical outcomes, Cox proportional hazard risk model or Fine and Gray model to compare incidence for outcomes between rivaroxaban versus dabigatran, and rivaroxaban versus VKA (standard and reduced doses), for hdPS matched patients, and all patients with hdPS adjustment.The analysis of healthcare costs during the drug exposure will be performed as an “intent-to-treat” analysis. Costs will be estimated according to treatment group from national health insurance and collective perspectives.

Documents

Study results

BROTHER_Study_report_1-year_follow-up_V3.0_Clean_20181120.pdf (3.88 MB)

BROTHER_Study_report_2-year_follow-up_V1.0clean_20181116.pdf (4.5 MB)

Study publications

Blin P, Fauchier L, Dureau-Pournin C, Sacher F, Dallongeville J, Bernard MA, La...

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Administrative healthcare records (e.g., claims)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No